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# RADIUM

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CHARLES H. VIOL, Ph. D.  
AND  
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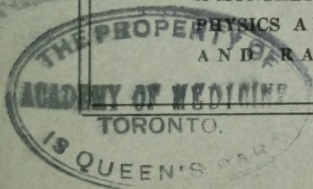
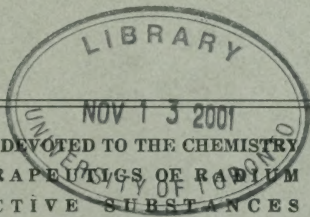
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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY  
PHYSICS AND THERAPEUTICS OF RADIUM  
AND RADIO-ACTIVE SUBSTANCES





# RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND  
THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D.  
with the assistance of collaborators working in the fields of  
Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. X

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## THE RESULTS OF TREATMENT OF BLADDER TUMORS\*

JOHN T. GERAGHTY, M. D.

Baltimore

The treatment of bladder tumors prior to 1910 was in almost all cases a surgical one, with an attempt at partial or complete removal of the growth. Whether the tumor was benign or malignant, operative procedure offered the only hope of cure or alleviation. The brilliant results obtained by Nitze in his endovesical treatment of bladder tumors were not duplicated by other urologists, as the skill necessary for the employment of his methods was not perfected. The introduction of fulguration by Beer and later the employment of radium are two procedures which have served radically to change our ideas, and have consequently affected our attitude in the selection of the proper treatment for any individual case.

When fulguration was first employed, the results obtained by different surgeons were apparently immeasurably superior to the results secured by old operative methods. It began gradually to be realized, however, that all vesical tumors were not amenable to this form of treatment, and that while certain tumors disappeared with surprising rapidity, others responded only after long and vigorous applications, while others again were not affected in the slightest degree.

In order to secure an explanation of the difference in the response to treatment, we have made a study of the pathology of the different tumors and tried to correlate the different types and their response or resistance to fulguration. The results of this study have shown that the tumors which respond most readily to fulguration belong to the benign papilloma

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\* From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

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type, while those which are not affected, or are often stimulated in their growth, are histologically papillary carcinoma. There is, however, an intermediate group of tumors, the malignant papilloma, which varies in its response to this treatment, some responding almost as readily as the purely benign type, while others approach in their resistance the true papillary carcinoma. The differentiation between the malignant papilloma and the papillary carcinoma may, in many cases, be extremely difficult, and, notwithstanding the histologic picture, the final diagnosis may be reached purely by the response to fulguration or radium. The employment of radium within the last few years has necessitated still further studies regarding the type of tumor in which this agent has proved valuable. As with fulguration, it has been learned by experience that certain tumors disappear under its influence, while others apparently are not affected by it.

Much confusion has always existed concerning the nature and pathology of bladder tumors. Most of this confusion exists as regards the papillary tumors which are the commonest of vesical neoplasms. Until a definite classification is adopted and a specific nomenclature employed, these inaccuracies will continue. For example, the use of the term "cancer" for the papillomatous, noninfiltrating types of tumor, even though there be histologically malignant changes present in the epithelium, is confusing, because experience has shown definitely that certain therapeutic measures suitable for one are wholly inadequate for the other. Frequently the surgeon in reporting the results of a given form of treatment for cancer may include in his series cases of malignant papilloma. The result of such a report leads to erroneous conclusions. A classification which has proved at least a satisfactory working basis is the following, because it is possible to correlate the histologic and clinical picture with the response to different therapeutic agents.

The papillary tumors may be classified as benign papilloma, malignant papilloma and papillary carcinoma. Papilloma is a name which common usage has popularized in medical literature, and it is used to denote a group of tumors having certain gross characteristics. The term "papilloma" has come to imply a pedunculated, papillary form of villous tumor springing from the mucous membrane of the bladder and being essentially composed of a branching connective tissue framework, lined by epithelium in several or many layers. Statistics prove conclusively that papilloma is by far the most frequent tumor of the bladder, and when it is further considered that practically all the papillary carcinomas represent an advanced malignant degeneration of tumors which in their early stages were papillomas, the preponderance of this type of vesical neoplasm can be appreciated.

The gross appearance of papillomas varies considerably, and there is no definite characteristic which will differentiate the benign from the malignant. In most instances it is impossible from the gross appearance to decide the character of the growth, so closely in general appearance do the benign and malignant papillomas resemble each other. The pedicle in the malignant papilloma is freely movable over the underlying mucosa, and there may be nothing in its appearance to reveal its malignant character. In the vast majority of cases, the differentiation between the benign and malignant papillomas can be made only by the most careful microscopic study, and it sometimes necessitates the examination of sections from various portions of the tumors. In the benign, the connective tissue axis is lined by an epithelium which has a palisade arrangement at the base and above this many layers of oval

longtailed cells which are uniform in size, shape and staining characteristics. Toward the surface the cells become flattened, and the most superficial are similar to the epithelium of the normal bladder mucosa. In the malignant, the arrangement of the epithelium is changed, and instead of being in regular, uniform layers, it is disordered. The individual cells are very irregular in size and shape, and take the stain with varying degrees of intensity. These variations from normal are even more evident in the nuclei. At times, owing to the lawless growth of the epithelium, the papillae fuse so that the regular papillary arrangement is destroyed. Not infrequently in the same field, papillae may be seen undergoing various degrees of alteration. In one portion the epithelium may have all the characteristics of the benign papilloma, but close by may be papillae in which epithelial changes characteristic of malignant papilloma are very evident.

The term "malignant papilloma" should be reserved for those tumors in which the malignant changes are confined to the epithelium, and in which there is no infiltration of the epithelium into the connective tissue framework. When the epithelium breaks through its basement membrane and begins to invade the axis of the papilla or its main stalk, it no longer should be considered a papilloma, but a papillary carcinoma.

In order to arrive at some conclusion as to what may be expected from the different forms of treatment, we have included in our studies only those cases which have been seen since January, 1911. This makes it possible to compare our results of the last six years in which recent procedures have been employed with the results obtained prior to this time when operative measures alone were used. From January 1, 1911, at which time fulguration began to be employed for the first time in our clinic, until April 1, 1917, 145 cases of bladder tumor have been observed. Of these there were 64 cases of papilloma, 74 of papillary carcinoma, 3 of adenocarcinoma, 1 of colloid carcinoma, 1 of cystic adenoma and 2 of multiple vesical polyps.

## THE TREATMENT OF PAPILLOMAS.

Of the sixty-five cases of papilloma in our series, thirty-four were treated by fulguration alone, the Oudin or unipolar current being almost exclusively used. In five of these, previous suprapubic excision had been performed and the tumors represented recurrences. In twenty-six of the thirty-four cases treated by fulguration, subsequent cystoscopic examinations were carried out, and in ten cases, or 29 per cent., recurrences were noted. In seven cases the recurrence was present in less than one year, in one case after one year, in one case after one and one-half years and in one case after two years. In three of these cases the recurrence was in the region of the original tumor, and in the remaining seven they were on portions of the bladder wall distant from the site of the primary tumor. Of the sixteen cases in which there was no recurrence, one patient was well for six years, one for five years, one for four years, three patients for three years, three for two years, two for one year and five for less than one year.

The recurrent tumors, with one exception, have all responded to fulguration like the original tumor. This one exception is of extreme interest.

Case 1.—This patient had a papilloma several centimeters in diameter just back of the ureteral orifice, which disappeared rapidly under fulguration. For several months after the disappearance of the tumor, the mucous membrane in the tumor-bearing area appeared perfectly healthy.

Shortly after, cystoscopy revealed a peculiar reddening and slight bulging of the mucous membrane in this region without ulceration or definite tumor formation. At first this was thought to be a localized inflammatory area. The process, however, seemed to spread, and a piece removed by the cystoscopic rongeur revealed an infiltrating carcinoma with the mucosa covering it practically intact. This is undoubtedly a case in which cancer cells from the malignant papilloma had metastasized into the deep bladder walls and there continued to grow after the original tumor had completely disappeared. This case really should be considered as a metastasis rather than a recurrence.

One other case is deserving of special mention because the recurrences continued over so long a period.

Case 2.—This patient, aged 52, was seen in February, 1912, with a large papillomatous tumor covering the left lateral wall and with several smaller tumors around the vesical orifice. The small tumors readily disappeared, but the large tumor responded only after months of vigorous and intense fulguration. Within a few months after the last vestige of the original tumor had disappeared, several recurrences the size of a pinhead were seen in widely separated portions of the bladder. These responded readily to fulguration. Since then the patient has been examined with the cystoscope on an average of about once a month, and practically at every examination small papillomas are found. During the last five years, probably several hundred tumors have been removed in this way. At the present time, the tendency to recurrence is just as active as it was five years ago, but it has been possible by watchful and persistent care to destroy the recurrence as fast as they form.

*Treatment by Radium and Fulguration.*—During the past two years, for papillomatous tumors which have shown histologic changes characteristic of the malignant papilloma or which were unusually resistant to fulguration, radium has been employed in combination with fulguration. Depending on the size of the tumor, varying amounts of radium have been employed, ranging from 200 to 1,000 milligram hours. Of the eighteen cases treated by this combination, in seven the tumors were multiple. Two patients discontinued treatment before the tumors had been removed. In the remaining sixteen cases, the tumors were completely destroyed. In all but one of these, subsequent cystoscopic examinations have been made, and in four cases, or 27 per cent., recurrences were found. In all four cases the recurrences were present in less than one year. The remaining eleven cases were free from recurrence for periods of time as follows: three for two years, four for one year, three for six months, and one for three months.

The following case illustrates the specific role which radium seems to play in rendering malignant papillomas, which have proved resistant to fulguration, amenable to this form of treatment.

Case 3.—A man, aged 75, had a papillomatous tumor 3 cm. in diameter just back of the trigon. Cystoscopically the tumor was pedunculated, with short stubby papillae. Microscopic examination of a piece of tissue removed showed the characteristic changes of malignant papilloma. The tumor was apparently in no way different, either cystoscopically or microscopically, from other tumors in which fulguration is effective. The tumor was fulgurated over a period of six months at biweekly intervals, and at the end of this time it was about three-fourths its original size. In the beginning of the treatment, the tumor decreased definitely but slowly, and finally it seemed to remain stationary

in size. Frequently a fulguration sufficiently vigorous to coagulate apparently the entire tumor mass was employed, but examination two weeks later, on the separation of the slough, would reveal the tumor apparently unchanged. Finally radium was applied directly to the surface of the tumor, both the beta and gamma rays being employed. These radiations totaled 600 milligram-hours and were carried out over a period of eight weeks, 103 mg. of radium being applied for one hour at approximately weekly intervals. At the conclusion of this radiation, the tumor showed no evident changes either in size or appearance. The tumor was now vigorously fulgurated, and disappeared completely after one treatment. The patient died six months later of pneumonia. Necropsy revealed no recurrence in the bladder and there were no metastases present.

Up to the present time there have been six other cases responding only slightly to fulguration which, after varying amounts of radium, have yielded readily to the high-frequency treatment. All of these cases were of the malignant papilloma type.

Another case of considerable interest is the following:

Case 4.—A man, aged 50, had two papillomatous masses on the anterior bladder wall which had received a large amount of fulguration elsewhere without any apparent improvement. The resistance to this type of treatment was confirmed by us. A course of radium was then employed which was followed subsequently by fulguration, the tumors apparently disappearing promptly. Cystoscopy one month later revealed a recurrence in the same area. This was treated in a manner similar to the other tumors, with disappearance. There was noted on cystoscopy after the disappearance of the tumor, in the region formerly occupied by it, a small shallow cuplike depression in the bladder wall, resembling a cellule. Examination three months later revealed another recurrence. The tumor occupied so ideal a position for resection that operation was decided on. When the bladder was exposed, a diverticulum was found at the point of the insertion of the urachus. This was filled with tumor, which readily explained the recurrences. The diverticulum communicated with the bladder by a narrow orifice and the tumors previously destroyed were implantations of the tumor concealed in the diverticulum.

*Treatment with Radium.*—In three cases the papillomas were treated with radium alone, and in all three cases the tumors treated disappeared under the influence of radium. One of these cases is of particular interest in that the patient had numerous malignant papillomas around the vesical orifice and a localized infiltrating papillary carcinoma involving the right ureteral orifice. Any operative procedure, short of complete cystectomy and prostatectomy, would have been useless. It was possible, however, to destroy the papillomas by means of radium within a few weeks, after which a resection of the papillary carcinoma, with transplantation of the ureter, was successfully carried out. The papillary carcinoma and other forms of infiltrating malignant tumor, in our experience, as will be considered later, have not responded to this form of treatment, and resection was consequently indicated. This case probably illustrates very well the possibilities of a combination of treatments for securing results practically impossible of attainment by any one procedure.

*Technic of Radium Applications.*—In this connection it may be well to outline briefly the technic we have followed in the application of radium to bladder tumors. The treatment in practically all cases has been

carried out with 103.7 mg. of radium element. In the majority of the treatments a fenestrated brass capsule has been employed and both the beta and gamma rays utilized. In other cases, however, the radium has been contained in a capsule of platinum 1.5 mm. in thickness, a screenage sufficient to filter out practically all of the irritating beta rays. The capsule containing the radium had been introduced into the bladder in the beak of an instrument not unlike the sheath of the irrigating cystoscope. These instruments permit the passage through them of an observation cystoscope by means of which the tumor may be viewed and the radium accurately placed on it. After the radium has been directed against the tumor, the instrument is held in a fixed position by means of a mechanical arm attached to the cystoscopic table. The radiations are usually given throughout the period of an hour at each seance and carried out from one to three times weekly, depending on the tumor and the reaction of the patient to the treatment.

*Treatment by Suprapubic Removal.*—This procedure was carried out in ten cases. In six of them the tumors were removed by the actual cautery and in four by resection. Of the former there were two recurrences in less than one year, while in the latter no recurrences were noted. It should be stated that in both cases in which recurrences were found the tumors were very extensive and occupied a large portion of the bladder wall. Of the patients treated by removal with the cautery, one has been well six years; one, two years; one, one year, and one for six months. Of those resected, three have been well five years, and one, one year.

#### PAPILLARY CARCINOMA.

In eighteen of the seventy-four cases of papillary carcinoma, the tumors were considered operable, and in all of them radical resections were carried out. In five cases the ureter was transplanted, and in one case both ureters were similarly treated. In these eighteen cases there was only one operative mortality, that being the case in which both ureters were transplanted. The death in this case occurred in the third week, being due apparently to pulmonary embolism. It has been possible to secure data concerning all of the eighteen patients. Eight have since died, and of the ten living, one has been well for six years, one for five years, one for four years, and seven for less than one year. It is noteworthy that recurrence in the suprapubic scar, which was a not infrequent sequela in our earlier operation, has not been observed in any of these cases. This is probably due to the greater care which has been exercised in preventing implantations during operation.

In fifty-six cases, or 75 per cent., the papillary carcinomas were so extensive that radical excision was considered impossible. In eleven of our extensive cases fulguration was employed, but aside from symptomatic relief, nothing was accomplished. In a few instances, it was possible to destroy enough of the tumor to give temporary relief from mechanical obstruction, while in certain of the cases, hemorrhage was relieved. In no instance was it possible completely to destroy the tumor.

*Treatment by Radium and Fulguration.*—In eleven cases a combination of radium and fulguration was used. The radium in every instance was applied directly against the tumor mass, and varying amounts, from a few hundred to several thousand milligram hours of radiation, were given. In the majority of cases both the beta and gamma rays were employed, but in the remaining the radium was heavily screened with suffi-

cient platinum to filter out practically all of the beta rays. The combination of radium and fulguration of this type of case in no instance caused the complete disappearance of the tumor, or, in fact, any marked effect on it. In some cases, however, some symptomatic relief was obtained.

*Treatment with Radium.*—In thirteen cases with extensive infiltrating carcinoma, radium alone was employed. The results in this series differ in no respect from the cases treated by the combination of radium and fulguration. As in the latter series, a number of cases were relieved symptomatically, but in no case was there complete disappearance of the tumor.

*Diagnosis.*—The study of our results strongly emphasizes the necessity of early differentiation of the papilloma from the papillary carcinoma, because the endovesical methods at our command have proved to be futile in the treatment of the latter type. On the other hand, these endovesical methods for the treatment of papilloma yield results incomparably superior to any of the more radical procedures. The differentiation of the benign and malignant papilloma, so far as treatment is concerned, is not so essential, for in the majority of the latter variety, fulguration proves most satisfactory. In the small group which proved resistant, the combination of radium and fulguration will accomplish the desired result.

The differentiation between the papillary carcinoma and the malignant papilloma is not always easy, but in the majority of cases cystoscopy, palpation, histologic examination of a portion removed and a consideration of symptoms, either alone or, as is usually the case, in combination, will furnish information sufficient to make an accurate diagnosis.

*Cystoscopy.*—It is surprising how frequently from cystoscopy alone one is able to distinguish the papilloma from the true carcinoma. While the pedicle of the papilloma is rarely distinctly visible, often the tumor mass can be seen to sway as a whole in the fluid, which indicates its pedunculated character; and at other times it is possible to view slightly beneath the mushroom-like edge of the tumor. It is impossible from the cystoscopic appearance of papillomas to determine whether they are benign or malignant. When, however, the malignant changes are so advanced that infiltration of the bladder wall has occurred, there are certain cystoscopic appearances which nearly always enable one to arrive at a fairly accurate diagnosis. The presence of necrosis in the papillae is indicative of carcinoma, and is usually associated with invasion of the underlying bladder wall. In the earlier stages, when the tumor has just begun to invade the bladder wall, it may not be possible cystoscopically to determine this point; but when the process is at all advanced, the tumor loses its pedunculated character and becomes sessile in type. Frequently, around the margin of the tumor is seen edema, or bullae, which are usually indicative of a cancerous invasion of the bladder wall below. At other times little tumor nodules can be seen beyond the main tumor growth. This again is indicative of cancer. While it is impossible definitely to describe all the appearances which serve to diagnosticate the papillary carcinoma from the malignant papilloma, the cystoscopist of experience is usually able to differentiate them, and it is interesting to note how frequently the cystoscopic diagnosis proves to be correct.

*Palpation.*—Occasionally, when the bladder is extensively involved with an infiltrating form of growth and the abdominal wall is thin and

soft, the hard, irregular mass can be detected. When malignant growths occur on the posterior wall of the bladder, or on the posterior lateral wall, rectal examination frequently gives most valuable information regarding the nature of the growth and its extent, and frequently determines the possibility of complete eradication by operative procedures. When the growth infiltrates the bladder wall, induration can be detected, and the extent of the bladder wall involvement can be more or less accurately mapped out. About 50 per cent. of bladder tumors occur on the posterior bladder wall in a position accessible to the examining finger. Sometimes not only the induration is detected in the bladder wall, but later the seminal vesicles are also involved, and still later the prostate. In rare instances, the growth may extend through the rectum and a rectovesical fistula may result. This complication occurred in three cases in our series. It may be safely said that marked induration of the bladder wall, which is felt through the rectum, is strong evidence of carcinoma. In the female, valuable information regarding the condition of the posterior bladder wall may be obtained by vaginal examination.

#### EXCISION OF A PIECE OF TUMOR FOR DIAGNOSIS.

For a number of years we systematically removed pieces of bladder tumor by means of the Young cystoscopic rongeur for the purpose of histologic examination. The information derived from this method would seem to furnish conclusive evidence of the nature of the tumor, and consequently enable one to select accurately the type of treatment best suited to the tumor in question. Unfortunately, the evidence derived is not always conclusive, because of the fact that the portion removed is not always a safe index of the character of the remainder of the tumor. The piece removed may show no, or very few, malignant changes, while other portions of the tumor may be definitely carcinomatous. When the piece of tumor excised shows, however, definite carcinoma, the employment of radical procedures suitable for the individual case should be adopted without delay, and time should not be lost in the employment of the usual endovesical methods of treatment. The excision of a piece of tissue will also prove of value in differentiating the different types of vesical tumors. It should be noted, however, that the removal of the tissue by this means has been criticized as increasing the risk of metastasis. This has not been our experience, and the information obtained frequently counterbalances the theoretically increased risk of metastasis.

#### SYMPTOMS.

It has also been our experience that when a severe, intractable cystitis is associated with bladder tumor, the tumor has proved practically always to be cancer.

In rare instances, when the cancerous process is very early, it may be impossible to determine this by the usual methods. In these cases it has been our custom to test out, as it were, the nature of the tumor by means of fulguration and radium. If the tumor does not show prompt response to this combination, it can be assumed that it is of a cancerous nature.

#### METASTASIS.

When the possibility of metastasis in a given case is considered, it is again important to know the type of vesical tumor concerned. In our series of sixty-four papillomas, 75 per cent. of which were malignant, four cases of metastasis were noted. In all four cases the tumor was a pedunculated papilloma, which in every instance disappeared completely

under fulguration alone, or fulguration and radium combined. In one case, evidences of metastasis did not develop for four years after the removal of the primary tumor, but in the interval a great many recurrences had been destroyed.

Of eighteen papillary carcinomas in which the carcinoma was considered sufficiently well localized to attempt resection, and in which it was possible completely to remove the local growth, seven patients have since died of cancer and one of intercurrent disease. Of those living, only three have been well for a period of more than four years. When the carcinoma is extensive and deeply infiltrates the bladder wall, metastases are usually present. It should be recognized, however, that at times most extensive involvement of the bladder may be present with negative findings at necropsy, so far as metastases are concerned. In three of our cases in which the tumor was so extensive that complete removal seemed impossible, and in which death occurred while under observation, no metastases were demonstrated postmortem.

#### CONCLUSIONS.

The results of our experience in the past six years may be thus summarized: It is essential to determine accurately the type of tumor in a given case, in order to select the treatment best suited to the particular type in question. The early recognition of papillary carcinoma is most essential, and the diagnosis being made, the tumor should be radically resected, if operable. In our experience fulguration and radium have proved valueless in the cure of this type of tumor.

In this connection, it should be emphasized that, following the complete removal of a papillary carcinoma by resection, a recurrence may develop which in some cases proves to be, in its early stages, a malignant papilloma, and in this stage will respond to fulguration, or to a combination of fulguration and radium. In three of our cases in which a papillary carcinoma was radically removed, recurrences were found later and destroyed, by fulguration in two cases, and by radium and fulguration in the third.

While the results following the use of radium in the infiltrating carcinomas have been disappointing, the response of the more resistant malignant papillomas to this agent has been most encouraging. Radium alone will unquestionably destroy both the malignant and the benign papillomas, and on account of its influence on the former makes possible their cure without the employment of radical procedures which would otherwise be necessary. It has been our custom, when the diagnosis of malignant papilloma had been made, to give a varying amount of radiation, dependent on the size of the tumor, and to follow this by fulguration. Some of our malignant papillomas, in which fulguration was first tried without success, radium has rendered readily responsive to this treatment. Indeed, several cases which have stubbornly resisted frequent and vigorous fulguration, after a course of radiation have responded promptly to this measure.

The development of the endovesical methods has rendered it possible to effect a cure in practically all cases of papillomas, and the employment of the more radical operative methods has not been productive of results at all comparable with those following the more conservative methods. With the exception of rare cases, in which an operative procedure is carried out, resection alone should be performed, because operation is indicated only when the tumor is a papillary carcinoma, and mere superficial destruction, as with the cautery, etc., will usually be futile.

## ABSTRACT OF DISCUSSION.

Dr. Edward L. Keyes, Jr., New York: As regards carcinoma of the prostate, I confess I have been a little more enthusiastic about "cures" than I am now. Without being cured these patients may stay in very good health, but even those who get brilliant results from a single treatment, like the two men shown here, have to be treated again and again, to keep those results good. Of course, the condition of the prostate itself is no index of the patient's general health. I saw a patient recently who was treated with radium elsewhere and whose prostate feels almost normal, but who is dying of carcinoma in his lumbar glands. But one would expect to cure patients captured early enough for radium treatment at a time when the carcinoma has not extended beyond the prostate.

Dr. Geraghty has noted that fulguration after radium works better than fulguration before radium. It seems possible that those tumors would have disappeared if he had been able to keep his hands off them for a sufficient number of months after the radium. I have seen a case of what Dr. Geraghty would call malignant papilloma improve very much in the second three months after a dose of radium.

Dr. William F. Braasch, Rochester, Minn.: As Dr. Geraghty has pointed out, the treatment of tumors of the bladder unquestionably has been greatly improved in recent years. It is reasonable to assume that in the first attempts to remove tumors by these less formidable measures a certain number of unsuitable cases would be treated, with consequent failures. If we were to judge the comparative value of non-operative methods from statistics of past years, the operative procedure would suffer very much by the comparison. This is illustrated in recent papers by Drs. Gardner and Young.

The improvement in surgical technic has been along several lines. First, the bladders are cleaned up. Many of the patients with bladder tumor have a coincident cystitis and pyelonephritis and should be treated prior to operation much the same as patients suffering with prostatic conditions. Second, the wound should be carefully protected at the time of operation to prevent infection. Third, resection with the cautery knife, is better than with the ordinary knife, and together with cauterization of the surrounding area, should preclude any infection of the wound area. Fourth, formerly the ureters were often transplanted into other portions of the bladder with poor success, and sometimes with the death of the patient. If the ureter is markedly diseased, as it frequently is, it may be simply ligated and dropped into the wound. In such cases the kidney is usually largely destroyed and the patient does not suffer much reaction.

With the last year or two I have frequently seen patients who had been fulgurated over long periods of time. One patient had had forty fulgurations in two years. When I cystoscoped him it was evident that he had carcinoma and that it was too late for resection. Undoubtedly the tumor could have been resected if the patient had been operated on earlier.

I wish to emphasize that if, after three or four fulgurations, and possibly after using radium, the tumor does not markedly decrease in size, there is no excuse for continuing such treatment, and surgical procedures should be used. We have tried radium alone in a few cases of carcinoma, but with poor results. I disagree with Dr. Geraghty when he says that if a tumor of the bladder cannot be resected there is no object in attacking it surgically. Unquestionably good results can be obtained by using a cautery and searing the tumor almost to the muscular wall.

Dr. G. G. Smith, Boston: I should like to bear witness to the efficiency of radium in one case which I have had under personal observation. About two years ago I operated on an elderly man and took out an adenomatous prostate and a papilloma of the bladder. He did very well for two years. About Christmas I cystoscoped him and found he had an infiltrating growth extending upward from the sphincter. I sent him to Dr. Barringer, who treated him with one application of radium. That was some six weeks or two months prior to this meeting. I cystoscoped him recently and the growth had entirely disappeared, as far as one could tell. There was some sloughing around the base of the bladder.

In regard to the treatment of diverticulum, there is one point in the technic. I am not sure whether it has been put on record or not. After a diverticulum has been freed outside of the bladder by dissecting around it, it is easier to cut off the diverticulum and to approximate the cut edge if the diverticulum is inverted so that it projects into the bladder. The cutting and suturing can then be done inside the bladder in a more accessible situation.

Dr. John T. Geraghty, Baltimore: With regard to Dr. Keyes' remarks about the disappearance of these tumors under radium, I think that is perfectly true. In some of the cases which have been allowed to go without fulguration the tumors have disappeared. We have used fulguration to cause a more rapid disappearance of the tumor. Those which disappeared under fulguration after irradiation would probably have disappeared under irradiation alone.

With regard to the technic of resection, we make it a rule to burn the tumor vigorously before attempting resection. As soon as the bladder is opened the whole tumor is destroyed down to the base. Whether one carries on the dissection by the knife or the cautery makes little difference. When one destroys the whole area thoroughly it amounts to resecting that area of the bladder wall.

With regard to the cases mentioned by Dr. Braasch, it has been my experience that the tumors which we can destroy by the cautery are tumors that practically always respond to fulguration and radium. Those cases with infiltration I do not think would be cured by destroying with the cautery. There are a few cases in which the tumor is a definite, infiltrating carcinoma with a pedicle, and that tumor must be resected. Cutting off the tumor through the mucosa at the pedicle with the cautery is probably just as efficient as a resection.

With regard to the remark that the mortality from resection should not be as high as 12 per cent., our mortality in twenty-two resections has been one death.

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## REVIEWS AND ABSTRACTS

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Henry K. Pancoast, M. D., (Philadelphia). Malignant Disease of the Throat and Sinuses. Jour. A. M. A., LXIX, September 22, 1917, pp. 980-982. (Review of Cases Treated by Radium and Roentgen Rays.)

"At the present time, no single method of treatment is adaptable to all cases of malignant diseases. Of the many procedures now employed, surgery has the widest adaptation in cases in which the growth is accessible and can be completely eradicated, with the possible exception of superficial epitheliomas in certain localities. In many instances, the lesions must be attacked by a combination of several of the procedures

now at our command. Radium and Roentgen rays, while by no means the only agents that may be employed in cases not suitable for operative procedures, have probably the widest field of application next to surgery. When large surfaces must be exposed, as in the treatment of mammary carcinoma with its many harbors of metastasis, and when intensive deep cross-fire radiation is essential, as in the treatment of mediastinal, abdominal or pelvic tumors, Roentgen therapy is the method of choice between the two agents. When growths originate in cavities such as the mouth, throat and ear, deep cross-firing by Roentgen rays, or possibly by radium, is an essential part of the treatment, but the possibility of adding to the dosage and to the efficiency of the treatment by direct local applications of radium has a distinct advantage."

"I have selected as a basis for this report a group of cases peculiarly adapted to combined radium and Roentgen treatment or to radium therapy alone. In each instance the direct application of radium to the primary growth was indicated, although not always followed, and cross-fire radiation by radium or Roentgen rays was employed for the effect on metastases or the primary lesion or both. Operation was either undesirable, or a complete extirpation of the growth was impossible. In the selection of the two agents employed, we now believe that when cross-firing is desirable or is possible only over a comparatively small and superficial area, rather large amounts of radium with heavy filtration can be used to better advantage than Roentgen rays. When the area is larger and the lesion deeper, Roentgen rays are indicated as the agent of choice."

"The outcome in the cases in this group was not successful in every instance, but the failures, of which there were more than are here reported, were of great assistance in the development of a more effectual technic which proved more efficacious in other cases. The clinical diagnosis was, in some instances, not confirmed by a pathologic examination of tissue, as the removal of a section was not always possible or desirable but the nature of the conditions was beyond question to all the consultants concerned."

*"Report of Cases: Case 1.—Sarcoma of the right tonsil with metastasis to cervical lymphatics.*—A man aged 47, referred by Drs. J. A. Babbitt and J. B. Deaver, had a marked enlargement of the lower part of the tonsil extending into the root of the tongue, with lymphatic enlargement under the ear the size of a small fist. The pathologic diagnosis was that of round-cell sarcoma. The growth was first noticed about six weeks before presentation. Treatment: Radium element, 110 mg., distance filtration, thirty-nine areas one and one-half hours each over face and neck, followed in a few days by 90 mg. in two platinum tubes buried in the growth at two points for twenty-five hours. This was not followed by sloughing. There was an immediate effect on the external growth, and the tonsil became about one-half the original size. At the end of two weeks a 50 mg. tube was buried in the tonsillar mass for twenty-four hours. Later experience with other cases proved that this should have been done at once. By the thirty-ninth day the reaction had subsided and external cross-firing, followed by burying a tube in the tonsillar mass was repeated, but with diminished dosage. At the end of fourteen weeks the tonsillar growth had disappeared and only a small mass the size of a walnut remained back of the angle of the jaw. This was excised by Dr. Deaver, and a 50 mg. tube of radium inserted for twenty-four hours. About two weeks later a very

rapid metastasis appeared in the front and base of the neck. Under combined radium and Roentgen applications this disappeared within twenty-four hours. The patient was also exhibiting signs of cerebral metastasis and died two weeks later. There was no recurrence in the neck or tonsil.

*Comment.*—Later experience demonstrated that: 1. This growth was too long in its disappearance and too much time was allowed for metastasis. 2. The growth should have been attacked more vigorously at the start when it was found not to subside more rapidly. (A tube of radium might have been inserted in the tonsillar mass at once. Only those cases responding promptly are likely to be cured.) 3. When there is decided cervical gland involvement in such cases, more distant metastases are likely to be present and treatment should be directed toward them."

*"Case 2.—Sarcoma of the left tonsil with metastasis to cervical lymphatics.*—In a patient referred by Dr. B. A. Randall, examination revealed a large sloughing mass involving the left tonsil and soft palate and almost closing the fauces, with lymphatic enlargement under the ear. This seemed a hopeless case. The patient was in a very weak condition and hardly able to swallow or speak. The Wassermann test proved negative, and there was no response to treatment with mercury and iodid. Treatment: Radium element, 90 mg., aluminum filter, 2 mm., was applied to twenty-nine areas both sides of neck, seventy-five minutes each. Immediate improvement was noticed, swallowing was easier and the patient could talk. Dr. Randall feared to adopt my suggestion to bury some radium in the tonsillar mass lest the sloughing already present should be increased. Later experience showed that this would probably not have occurred. In three weeks the tonsillar mass was about one-third smaller and the external glandular mass had nearly disappeared. Although a second series of external applications was made a week later the patient died soon afterward."

*Comment.*—This case is cited as an example of the effect of cross-fire radium radiation and its value as a part of the technic. Although this case was probably hopeless from the start, a more decided influence on the primary growth could no doubt have been obtained by direct applications in addition."

*"Case 3.—Carcinoma of the left tonsil.*—In a patient referred by Drs. George P. Muller and W. Estell Lee, examination revealed a large sloughing mass in the region of the left tonsil, with no apparent cervical glandular metastasis. Treatment: Radium in platinum capsule was buried twenty-four hours in the growth by Dr. Muller and repeated in three weeks, and again at the end of seven weeks. Four weeks later a short superficial application was made to the only remaining portion of the growth and again about peritonsillar tissues and of the neck, and it was thought that extensive sloughing from too vigorous treatment was the cause. The patient died shortly after this, and necropsy disclosed no evidence of local recurrence. The unfortunate terminal phase of the case was found due to a very rapid and deep extension of the growth into the neck posteriorly."

*Comment.*—This case, one of our earliest ones, demonstrated the fact that too much attention was paid to the primary growth and too little to possible metastases, which must always be suspected, even though not apparent. We must also recognize the possibility of stimulation of distant parts of the growth beyond the reach of the destructive dosage. Even though this was a case of carcinoma, and not so amen-

able to treatment as sarcoma, it proved a valuable lesson in the perfection of our technic in connection with subsequent cases of this kind."

"Case 4.—*Sarcoma of left tonsil*.—In a patient on the service of Drs. Charles H. Frazier and George P. Muller, examination revealed a large tonsillar growth extending past the midline. There was no sloughing, but there was probably some cervical glandular metastasis which became visible later. Treatment: Radium element, 50 mg., in platinum tube was buried twenty-four hours in the tonsillar mass by Dr. Muller. This was repeated ten days later and smaller amounts were similarly applied four times during the following three months. When seen at the end of five months, all evidences of the growth had disappeared, but there was still some resistance under and behind the angle of the jaw. Cross-fire radiation was employed over this area and the side of the neck, and repeated seven weeks later as a precautionary measure. The patient is now perfectly well at the end of two years, and during this time has been a useful citizen engaged in the making of heavy guns."

"Comment.—This was also one of our early cases, and had the growth been carcinoma instead of sarcoma we probably should not have succeeded. Comparing this with the cases that follow, it will be seen that implantation alone is insufficient for a rapid cure; which is far more safe than the slow reduction of a growth over a period of several weeks or months."

"Case 5.—*Sarcoma of the left tonsil with metastasis to cervical lymphatics*.—A man, aged 74, referred by Drs. R. E. Buckley and John B. Deaver, had a large growth in the left tonsillar region extending to the midline, with no sloughing. There was very evident glandular enlargement in the neck under the ear. Treatment: Radium element, 110 mg., aluminum filter, 2 mm., was used in cross-firing from both sides of the face and neck and a tube of 35 mg. in a platinum capsule was implanted eighteen hours in the tonsillar growth. The patient was sent home and returned for inspection in sixteen days. No evidence of the growth remained. A second series of cross-fire applications was administered at the end of three weeks and a third at the end of fifteen weeks, although there was no recurrence. A fourth series will be given later."

"Case 6.—*Postpharyngeal lymphosarcoma with metastasis to cervical lymphatics*.—A man, aged 56, referred by Drs. Howard Whittaker and Francis R. Packard, had a large mass completely occluding the fauces and apparently springing from the pharynx back of and above the left tonsil. It bulged into the mouth, but more into the posterior nares, and pushed the soft palate downward. The eustachian tubes were obstructed, breathing was difficult, and only liquids could be swallowed. Punctures by another physician showed no suppuration. In addition, there was a large glandular swelling below and back of the angle of the jaw about the size of an egg. The Wassermann test was negative. The patient had lost 40 pounds in four weeks. Treatment consisted of external application over the *left* side of the face and neck by 110 mg. of radium element, 2 mm. aluminum filter, thirty-five areas, one hour each; 35 mg. radium in platinum tube was implanted eighteen hours in growth in throat, and cross-firing by Roentgen rays was applied through the *right* side of the face and neck and the thorax. In less than two weeks all evidences of the growth had disappeared. The external radium and Roentgen applications were repeated a month later, and a third series was administered in another month. At present, three and one-half months

after the first treatment, the patient is apparently entirely well and has gained 41 pounds. Another series of applications will be given later."

"*Comment.*—This patient received as vigorous treatment as it is possible to administer. There was no sloughing in the throat, and the skin reactions, while quite marked, were well within the bounds of safety."

"*Case 7.—Sarcoma of left turbinates and antrum.*—A woman, aged 51, on the service of Dr. Charles H. Frazier, University Hospital, had large turbinates blocking the left side of the nose, with granular surface and not shrinking under cocain or epinephrin. Roentgenogram showed dense clouding of the left antrum. The pathologic report on section removed was sarcoma. Treatment: Radium element, 75 mg., in two platinum tubes was placed twenty-four hours above and below the lower turbinate. About two months later, 25 mg. were again inserted in two areas twenty-four hours each. The antrum was now open. A month later the antrum still contained sarcomatous tissue, and there were some metastatic enlargements in the neck. Applications were made over these glands, over the antrum and in the antrum, for the last time. Later another series over the cervical enlargements failed to affect them materially, and a block dissection was performed nearly eight months after the first admission. Subsequently a post-operative series of applications was made. The patient was last seen, April 1, 1917, twenty months after beginning treatment, and there has been no recurrence."

"*Comment.*—Experience with this and similar cases has shown that implantation alone is not always sufficient to control such a growth that is not very definitely localized. It is a wise precaution to employ radium or Roentgen-rays over the neck even when the primary growths is in such a locality as in this case."

"*Case 8.—Carcinoma of the left auditory canal, with metastasis to cervical lymphatics.*—A woman, aged 54, referred by Dr. B. A. Randall to the service of Dr. Charles H. Frazier, had a sloughing red mass projecting from and entirely occluding the external auditory canal. Under the ear there was a metastatic cervical enlargement the size of a walnut. The pathologic report was carcinoma. Treatment: Radium element, 25 mg., in a platinum tube was inserted twenty-five hours into the mass in the auditory canal. The cervical enlargement was treated by cross-fire radium radiation. In five weeks the latter had entirely disappeared, and the canal was open. The same treatment was repeated. Five weeks later, Dr. Randall reported too much granulation tissue in the canal, and a radium tube was again inserted for twenty-eight hours. There was no recurrence in the neck. When last seen, about one year after admission, the canal was clear, though there was still a little discharge, and there was no cervical enlargement."

"*Conclusions.*—1. In the treatment of inoperable malignant growths originating in cavities such as the mouth, throat and ear, radium therapy is an extremely valuable adjunct for the reason that it can usually be applied directly to the growth, which is more or less inaccessible to direct Roentgen-ray exposure. This alone is not sufficient, and the growth should also be attacked from every possible direction by cross-firing either by radium or by Roentgen rays or both. Any nearby area in which metastasis is likely to occur should also be exposed."

"2. When implanted directly into sarcomatous tissue, radium usually causes little or no sloughing if the growth responds promptly."

"3. It is advisable to produce as rapid subsidence of the growth as

possible in order to minimize the possibility of metastasis during the period of treatment."

"4. Our experience has seemed to prove that growths insufficiently treated at the periphery may be stimulated to more rapid proliferation at this portion."

"5. Sarcomatous growths, especially in the tonsillar region, are more amenable to treatment than carcinomas."

"6. It would be best to continue treatment for some time after the apparent complete disappearance of the growth."

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Rollin H. Stevens, M. D., (Detroit, Mich.) *The Blood in Cancer under Roentgenotherapy.* The American Journal of Roentgenology, IV, pp. 215-246, May, 1917.

"The object of this study was primarily to determine the relationship between changes in blood counts of cancer patients being treated with roentgen rays and the progress of the case." "This contribution is not intended as a final report, and consequently no final conclusions could safely be drawn from the few cases reported. There is a great need for further research work along this line, not only in cancer but in other diseases and in normal individuals exposed to the roentgen rays. In this research, however, it is quite evident that complete blood counts and hemoglobin estimation should be made almost daily over a considerable period of time—a very large undertaking—before fair comparisons can be made." "The data at hand would seem to justify the following conclusions."

"(1) Roentgen rays, applied in repeated large doses, with deep penetration, profoundly affect the erythrocytes of human beings, contrary to most of the reported experiments on small animals."

"(2) For the first few days, the lymphocytes are suppressed or destroyed by large doses of roentgen rays in the treatment of cancer. In favorable cases, this is followed by a reaction with lymphocytosis between the third and seventh days, which may continue almost uninterruptedly till the fourteenth day, or it may stop shortly after the seventh day and reappear more strongly and persistently on or about the fourteenth day. We note the striking similarity between this and the action of the rays on the blood of lower animals."

"(3) There is a strong resemblance between the curves of these lymphocytic reactions and those which constitute the opsonic index. The treatment should probably not be repeated until the reaction is over."

"(4) The repetition of the dose should probably be governed by the reactions in the blood as well as in the skin, the former being much more sensitive than the latter."

"(5) In some cases of cancer, the roentgen rays tend to stimulate a general (though probably temporary) immunity. The action of the roentgen rays in cancer, therefore, would appear to be twofold; local, by its destruction of disease cells; and general, by stimulating lymphocytosis and, consequently, resistance."

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